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| Substitute for form 1449/PTO<br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br><i>(Use as many sheets as necessary)</i> |   |    |   | <b>Complete if Known</b> |                        |
|  |   |    |   | Application Number       | 10/540,084-Conf. #7531 |
|  |   |    |   | Filing Date              | April 7, 2006          |
|  |   |    |   | First Named Inventor     | Mary Collins           |
|  |   |    |   | Art Unit                 | 1644                   |
|  |   |    |   | Examiner Name            | I. I. Ouspenski        |
| Sheet  | 1 | of | 3 | Attorney Docket Number   | M0274.70042US02        |

| U.S. PATENT DOCUMENTS |                          |  |                                   |  |   |
|-----------------------|--------------------------|--|-----------------------------------|--|---|
| Examiner<br>Initials* | Cite<br>No. <sup>1</sup> | Document Number                          | Publication<br>Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines, Where<br>Relevant Passages or Relevant<br>Figures Appear |
|                       |                          | Number-Kind Code <sup>2</sup> (if known) |                                   |  |   |
|                       |                          | US 2005/0180969                          | 08/18/2005                        | Hardy et al.                                       |   |

| FOREIGN PATENT DOCUMENTS |                          |   |                                   |  |   |                |
|--------------------------|--------------------------|---|-----------------------------------|--|---|----------------|
| Examiner<br>Initials*    | Cite<br>No. <sup>1</sup> | Foreign Patent Document   | Publication<br>Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines, Where<br>Relevant Passages or Relevant<br>Figures Appear | T <sup>6</sup> |
|                          |                          | Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known) |                                   |  |   |                |
|                          |                          | WO 04/0568754 A1  | 07/08/2004                        | Wyeth, et al.                                      |   |                |

| NON PATENT LITERATURE DOCUMENTS |                          |   |                |
|---------------------------------|--------------------------|---|----------------|
| Examiner<br>Initials            | Cite<br>No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>2</sup> |
|                                 |                          | ANASPEC Online Catalog (Catalog No. 54662), "Anti-PDCD1 (CT)."<br><a href="http://www.anaspec.com/pdfs/54662.pdf">www.anaspec.com/pdfs/54662.pdf</a>  |                |
|                                 |                          | ANSARI et al., 2003, "The Programmed Death-1 (PD-1) Pathway Regulates Autoimmune Diabetes in Nonobese Diabetic (NOD) Mice," J. Exp. Med. 198: 63-69.  |                |
|                                 |                          | BENNETT et al., 2003, "Program Death-1 Engagement Upon TCR Activation Has Distinct Effects on Costimulation and Cytokine-Driven Proliferation: Attenuation of ICOS, IL-4, and IL-21, But Not CD28, IL-7, and IL015 Responses," J. Immunol. 170: 711-718.        |                |
|                                 |                          | BLAZER et al., 2002, "PD-1 Engagement Provides and Inhibitory Signal Which Downregulates T Cell Alloresponses In Vivo," Blood 100: 72a, Abstract No. 261.   |                |
|                                 |                          | CARRENO et al., 2002, "The B7 Family of Ligands and Its Receptors: New Pathways for Costimulation and Inhibition of Immune Response," Annu. Rev. Immunol. 20: 29-53.  |                |
|                                 |                          | CURETECH Press Release, 2007, "CureTech announces receipt of a Notice of Allowance from the US Patent and Trademark Office"   |                |
|                                 |                          | CURETECH, <a href="http://www.curetechbio.com/?TemplateID=29&amp;PageID=145&amp;TemplateType=14">http://www.curetechbio.com/?TemplateID=29&amp;PageID=145&amp;TemplateType=14</a>   |                |
|                                 |                          | DAVIES et al., 1996, "Affinity Improvement of Single Antibody VH Domains; Residues in All Three Hypervariable Regions Affect Antigen Binding," Immunotechnology 2: 169-179.   |                |
|                                 |                          | DE KRUIF et al., 1995, "Selection and Application of Human Single Chain Fv Antibody Fragments from a Semi-synthetic Phage Antibody Display Library with Designed CDR3 Regions," J. Mol. Biol. 248, pp. 97-105.  |                |
|                                 |                          | DESMYTER A. et al., 2001, "Antigen Specificity and High Affinity Binding Provided by One Single Loop of a Camel Single-Domain Antibody", The Journal of Biological Chemistry, Vol.  |                |

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|  |  |  |
|--|--|--|
|  | 276, No. 28, pp. 26285-26290.  |  |
|  | HOLLING, T. et al., 2004, "Function and Regulation of MHC Class II Molecules in T-Lymphocytes: Of Mice and Men," Human Immunology 65: 282-290.   |  |
|  | ISHIDA Y. et al., 1992, "Induced expression of PD-1, a novel member of the immunoglobulin gene superfamily, upon programmed cell death," EMBO Journal, 11:11, pp. 3887-3895  |  |
|  | JIRHOLT. P. et al., 1998, "Exploiting sequence space: shuffling in vivo formed complementarity determining regions into a master framework," Gene, 215, pp 471-476.  |  |
|  | LADNER et al., 2007, "Antibodies cut down to size," Nat Biotechnol. Aug;25(8):875-7.   |  |
|  | LEVI et al., 1993, "A Complementarity-Determining Region Synthetic Peptide Acts as a Miniantibody and Neutralizes Human Immunodeficiency Virus Type 1 In Vitro," Proc. Natl. Acad. Sci., 90: 4374-4378.                        |  |
|  | MARKS, J. D. et al., 1992, "By-Passing Immunization: Building High Affinity Human Antibodies by Chain Shuffling," Bio/Technology, Vol. 10, pp. 779783.   |  |
|  | MAYNARD J. and GEORGIU G., 2000, "Antibody Engineering," Annu. Rev. Biomed. Eng, 02 pp. 339-76.  |  |
|  | NISHIMURA, H. et al., 1999, "Development of Lupus-like Autoimmune Diseases by Disruption of the PD-1 Gene Encoding an ITIM Motif-Carrying Immunoreceptor," Immunity. Vol. 11, pp. 141-151.                                     |  |
|  | QIU et al., 2007, "Small antibody mimetics comprising two complementarity-determining regions and a framework region for tumor targeting," Nat Biotechnol. 2007 Aug;25(8):921-9. Epub.   |  |
|  | REITER, Y et al., 1999, "An Antibody Single-domain Phage Display Library of a Native Heavy Chain Variable Region: Isolation of Functional Single-domain VH Molecules with a Unique Interface," J. Mol. Biol. 290, pp. 685-698. |  |
|  | SÖDERLIND, E. et al., 2000, "Recombining germline-derived CDR sequences for creating diverse single-framework antibody libraries," Nature Biotechnology, Vol 18, pp. 852-856.  |  |
|  | SÖDERLIND, E. et al., 1999, "Complementarity-determining region (CDR) implantation: a theme of recombination," Immunotechnology, 4, pp. 279-285.   |  |
|  | WARD et al., 1989, "Binding Activities of a Repertoir of Single Immunoglobulin Variable Domains Secreted from Escherichia Coli," Nature 341: 544-546   |  |
|  | WELLING, et al., 1991, "A Ten-Residue Fragement of an Antibody (Mini-Antibody) Directed Against Lysozyme as Ligand in Immunoaffinity Chromatography," J. Chromatography, 548: 235-242.   |  |
|  | WILLIAMS et al., 1989, "Development of Biologically Active Peptides Based on Antibody Structure," Proc. Natl. Acad. Sci. 86: 5537-5541.  |  |
|  | XU J. L. and DAVIS M. M., "Diversity in the CDR3 Region of V <sub>H</sub> is Sufficient for Most Antibody Specificities," Immunity, Vol 13, pp. 37-45.   |  |
|  | ZHONG, X. et al., 2004, "Suppression of expression and function of negative immune   |  |

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|--|--|---|--|
|  |  | regulator PD-1 by certain pattern recognition and cytokine receptor signals associated with immune system danger," Int'l Immunology, 16:8, pp. 1181-1188. |  |
|  |  | Accession No. Q15116 (2003)   |  |
|  |  | Accession No. NM_008798 (2003)  |  |

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